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[Continued on next page]

(54) Title: NON-CONSTANT PRESSURE INFUSION PUMP
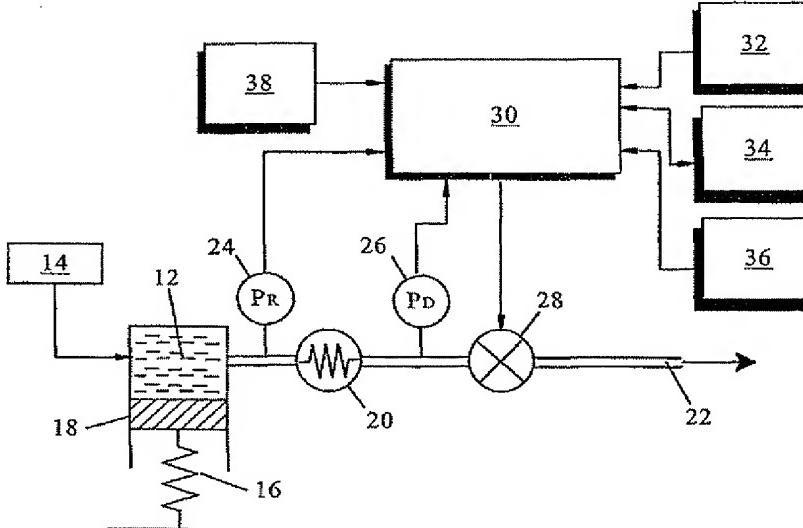
(57) Abstract: The present invention relates to an implantable infusion pump having a refillable infusate reservoir in fluid communication with a delivery site via a flow path. This flow path includes a flow resistance. The infusion pump includes a sensing device(s), positioned relative to the flow path, to provide data regarding a flow rate along the flow path. The infusion pump effects a division of a total flow period into at least a plurality of unit doase periods, each unit doase period effeting delivery of a unit dose of infusate. The cumulative effect of delivery the total numer of unit dose periods is the delivery of a desired dose over the total flow period. The present invention permits a reservoir pressure to vary over any portion of total flow period but effects a constant-pressure state over each unit dose cycle.

NON-CONSTANT PRESSURE INFUSION PUMP

FIELD OF THE INVENTION

The present invention relates to an implantable
infusion pump, and in particular, to an infusion pump
5   capable of effecting a precisely controlled (constant
or variable) fluid flow delivery rate, independent of a
constant reservoir pressure.

BACKGROUND OF THE INVENTION

Modern implantable infusion devices, or
10   implantable pumps, for delivering an infusate (e.g.,
medicaments, insulin, etc.) commonly have a rigid
housing that maintains a collapsible infusate
reservoir. The housing includes a needle-penetrable
septum that covers a reservoir inlet. A flow passage
15   is provided between the reservoir and an exterior
surface of the device. At the flow passage outlet, a
flexible delivery catheter is provided.

These devices are implanted at a selected location
in a patient's body so that (i) the inlet septum is
20   proximate to the patient's skin and (ii) a distal end
of the catheter is positioned at a selected delivery
site. Infusate can then be delivered to the infusion
site by controlling the flow of such fluid from the
device infusate reservoir into the delivery catheter.
25   When the infusate reservoir becomes empty, the
reservoir is refillable through the reservoir inlet by
injecting a new supply of infusate through the
apparatus' inlet septum. Due to the location of the
device in relation to the skin of the patient,
30   injection can be readily accomplished using a
hypodermic needle (or cannula).

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Infusate is expelled from the reservoir to an infusion site by collapsing the reservoir. Some infusion pumps use an electrically powered mechanism to "actively" pump infusate from the infusate reservoir

5   into the delivery catheter. Examples of these types of "active pumping" devices include so-called peristaltic pumps (e.g., SynchroMed[®] implantable pump from Medtronic, Inc., Minneapolis, Minn.) and accumulator-type pumps (e.g., certain external infusion pumps from

10   Minimed, Inc., Northridge, Calif. and Infusaid[®] implantable pump from Strato/Infusaid, Inc., Norwood, Mass.). These devices have certain advantages; however, such devices have a large disadvantage in that they use relatively large amounts of battery power to

15   effect infusion. Given that batteries tend to add bulk and weight and their replacement requires surgical intervention, it is very desirable to minimize power consumption in implantable infusion pumps.

Another type of implantable pump that is typically

20   much more electrically efficient uses a passive pumping mechanism. In fact, certain of these devices can be constructed and operated without any electrical power at all. A passive pumping mechanism generally consists of a means of pressurizing the infusate reservoir and a

25   means of restricting the fluid flow. All of these devices operate under the principle that the fluid flow rate (Q) is directly proportional to a pressure difference (ΔP) between the infusate reservoir interior and the delivery site and inversely proportional to the

30   total flow resistance provided by the fluid passage and delivery catheter (collectively (R)), wherein

$$Q = \Delta P \div R$$

A practical pump must have a predictable flow rate (Q). To achieve this goal, conventional designs have strived to develop substantially constant pressure

5   sources.

The first means of developing such a "constant pressure source" includes using a two-phase fluid, or propellant, that is contained within the rigid housing and is further confined within a fluid-tight space

10 adjacent to the infusate reservoir. Pumps constructed in this manner are called "gas-driven" pumps.

The propellant is both a liquid and a vapor at patient physiological temperatures, e.g., 98.6 °F, and theoretically exerts a positive, constant pressure over

15 a full volume change of the reservoir, thus effecting the delivery of a constant flow of infusate. When the infusate reservoir is expanded upon being refilled, a portion of such vapor reverts to its liquid phase and thereby maintains a state of equilibrium between the

20 fluid and gas states at a "vapor pressure," which is a characteristic of the propellant. The construction and operation of implantable infusion pumps of this type are described in detail, for example, in U.S. Patent Nos. 3,731,681 and 3,951,147. Pumps of this type are

25 commercially available, for example, Model 3000™ from Arrow International, Reading, Penn. and IsoMed® from Medtronic, Inc., Minneapolis, Minn.

Gas-driven infusion pumps typically provide an electrically efficient means to deliver a flow of

30 infusate throughout a delivery cycle. However, such infusion pumps depend upon a constant pressure source,

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wherein the output fluid flow rate is directly
proportional to a propellant-reservoir pressure. If
the propellant-reservoir pressure varies, then so will
the fluid flow rate and the drug delivery rate.

5   The propellant-reservoir pressure of conventional
gas-driven infusion pumps are susceptible to changes in
ambient temperature and pressure. This, in turn, makes
the fluid flow rate such devices susceptible to changes
in ambient temperature and pressure. Such changes in

10 drug infusion rates are undesirable and, in certain
situations, unacceptable.

Circumstances readily exist where either ambient
temperature or pressure can rapidly change a
significant amount. For example, the reservoir

15 pressure of some conventional gas-driven pumps can
change as much as 0.5 psi for each 1°F change in body
temperature. Thus, for example, assuming a pump
driving force of 8 psi at 98.6°F, a fever of only
102.6°F can result in a twenty-five percent (25%)

20 increase in propellant-reservoir pressure and thus, a
corresponding (or larger) increase in an fluid flow
rate. In addition, changes in environmental
temperature affect the infusate viscosity as well as
the vapor pressure produced by the propellant, thereby

25 further increasing the pump's susceptibility to
temperature.

An even more serious situation results from
changes in ambient pressure. Although minor variations
in ambient pressure at any given location on earth may

30 not significantly affect delivery flow rates, with
modern modes of transportation, a patient can rapidly
change altitude during travel, such as when traveling

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in the mountains or when traveling by plane. In a like
manner, a patient can experience a rapid change in
pressure when swimming or diving.

The rigid housing of the conventional, gas-driven
5   infusion pump provides an absolute constant-internal
pressure (P_R) (at constant temperature) independent of
external pressures. However, largely due to compliance
by the lungs and venous circulatory system, hydrostatic
pressure within the human body closely follows ambient
10 pressure (P_D).

The net effect is that the pressure differential
$(\Delta P = P_R - P_D)$ in conventional gas-driven pumps changes
linearly with ambient pressure. Consequently, a
delivered infusate flow rate can increase as much as
15 forty percent (40%) when a patient takes a common
commercial airline flight.

To overcome these practical circumstances, some
conventional gas-driven infusion devices have been
provided with elevated reservoir pressures. The
20 increased reservoir pressures are not intended to
prevent variations in a constant pressure delivery but
are intended to mitigate their effect. In particular,
for any given change of pressure, the effect on flow
rate is effectively lessened if the total percentage of
25 pressure change (relative to the reservoir pressure)
can be reduced. These infusion devices possess
undesirable attributes in that refilling operations are
more difficult and the high-pressure vessels, which
form the pump housing structures, must necessarily be
30 stronger and are therefore more susceptible to
manufacturing problems.

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Another method of attempting to produce a constant
pressure source and thereby more accurately controlling
a rate of fluid delivery is to incorporate a pressure
regulator, such as that disclosed in U.S. Patent No.
5   4,299,220. The pressure regulator described therein,
which is positioned between the infusate reservoir and
delivery catheter, uses a diaphragm valve to maintain a
constant pressure differential (ΔP) across the fluid
flow restrictor. In addition to increasing the
10   operational complexity of such a pump mechanism and the
volume of a fluid path extending therethrough, the
pressure regulator may, depending upon device
configuration, subject infusate solutions to high local
shear stresses, which may alter the chemical or
15   therapeutic properties of certain infusates.

An alternative method for attempting to produce a
constant pressure source and thereby more accurately
controlling a rate of fluid delivery, as well as
addressing the susceptibilities of the two-phase pumps
20   to ambient temperature and pressure, is proposed in
U.S. Patent No. 4,772,263. Specifically, in place of
the conventional rigid enclosure that maintains a two-
phase fluid, the disclosure teaches forming the fluid
reservoir between a rigid portion (which maintains at
25   least the inlet septum) and a flexible drive-spring
diaphragm. The spring diaphragm is exposed to the body
of the patient and the pressure therein. The spring
diaphragm creates a more desirable "relative" (as
opposed to an absolute) pressure source. By exposing
30   the spring diaphragm to the pressures inside the body
it is possible for the pump to respond and react to

changes in ambient pressure so that ΔP is unaffected.
Likewise, it is possible to construct the spring
diaphragm so that the pressure that it generates is not
affected by changes in ambient temperature. While this
5   configuration offers practical performance advantages,
this design offers a unique configuration that may not
be adopted by all constant flow pump designs.

Accordingly, a need exists for an electrically
efficient system to enable a controllable (constant or
10 variable) fluid flow delivery rate independent of
either a constant reservoir pressure or external
conditions that may otherwise result in undesirable or
unpredictable output fluid flow variations.

SUMMARY OF THE INVENTION

15 An object of the present invention is to provide
an implantable infusion device with a non-constant
reservoir pressure (over at least a portion of the flow
cycle) that controls fluid flow across a fluid flow
restrictor (with or without other fluid control
20 elements) by dividing a greater dose cycle into a
series of (smaller) unit dose cycles over which the
reservoir pressure is substantially constant.

Another object of the present invention is to
provide an electrically efficient implantable infusion
25 device, having a convenient pressure reservoir, that is
capable of delivering a prescribed dosage of a fluid
infusate independent of either a constant reservoir
pressure, ambient temperature or pressure, changes in
device performance, or infusate properties.

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Another objective of the present invention is to
provide an implantable infusion device that is simpler
in construction.

The present invention is directed to a controlled-
5   rate infusion device for implantation in a living body.
The infusion device includes a collapsible infusate
chamber, an energy source to collapse the chamber, and
an outlet flow path extending between the chamber and a
device outlet. The infusion device further includes at
10   least one flow restrictor, a controller, at least one
valve or variable flow restrictor to selectively alter
a flow resistance of the outlet flow path, and at least
one pressure sensing device. The pressure sensing
device(s) are positioned relative to the outlet flow
15   path as well as about the flow resistance (i.e., any
combination of flow restrictors and/or valves). The
controller is adapted to control an operation of the
valve (or variable flow restrictor) based on measured
value(s) obtained by the pressure sensing device(s).

20   In another aspect, the present invention is
directed to a controlled-rate infusion device for
implantation in a living body. The infusion device
includes a collapsible infusate chamber, an energy
source to collapse the chamber, and an outlet flow path
25   extending between the chamber and a device outlet. The
infusion device further includes a controller, a valve
(or variable flow restrictor) to selectively obstruct
the outlet flow path, and one or more pressure sensing
devices. The pressure sensing devices are positioned
30   relative to the outlet flow path as well as about the
flow resistance. The controller is adapted to assess
whether output flow from the device is undesirably

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restricted based on measured values obtained from the
pressure sensing devices.

Another aspect of the present invention is
directed to a method for controlling infusate output
5   from an implantable-infusion device for a prescribed
dose period. The device includes a collapsible
infusate chamber, an energy source to collapse the
chamber, and an outlet flow path extending between the
chamber and a device outlet, and the outlet flow path
10   includes a restrictor network, which includes an
occlusion device to selectively and at least partially
occlude the outlet flow path. The method includes the
steps of: (i) dividing the prescribed dose period into
a plurality of unit dose periods, wherein each unit
15   dose period is defined by an open-close cycle of the
valve; and (ii) modifying a duty cycle of the open-
close cycle of the valve so as to maintain a prescribed
output volume (i.e., a unit dose) for each unit dose
period.

20   Another aspect of the method for controlling
infusate output from an implantable infusion device can
include, independent of or in cooperation with other
aspects of this method, measuring an infusate pressure
differential across the restrictor network (or a
25   portion thereof). Thus, the step of modifying the duty
cycle is performed in accordance with a measured
infusate pressure differential.

Another aspect of the method for controlling
infusate output from an implantable infusion device can
30   include, independent of or in cooperation with other
aspects of this method, actuating the valve so as to
effect a change in an occluded state of the outlet flow

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path. During or proximate to such actuation, a transient pressure profile on one side of the valve is measured, thus enabling an assessment of the performance of the valve, fluid path, flow restrictor

5   and any other elements of the flow control system or flow path.

Another aspect of the method for controlling infusate output from an implantable infusion device can include, independent of or in cooperation with other

10 aspects of this method, measuring an infusate temperature. Thus, the step of modifying the duty cycle is performed in accordance with a measured infusate temperature.

Another aspect of the present invention is that an

15 output flow rate of a controlled rate pump can be changed by "resetting," or programming, such output flow rate. This resetting operation can be accomplished using non-invasive (e.g., magnetic switch, radio-frequency telemetry) or invasive methods (e.g.,

20 transcutaneous trocar). In this way, the methods and devices described herein can be used to construct a programmable pump, the flow rate of which can be manually or automatically (responsive to a clock, sensor, or other data input) modified to any of various

25 beneficial patterns.

Other objects and advantages of the present invention will be apparent to those of ordinary skill in the art having reference to the following specification together with the drawings.

30 **BRIEF DESCRIPTION OF THE DRAWINGS**

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In the drawings, like reference numerals and
letters indicate corresponding parts throughout the
several illustrations:

FIGURE 1 schematically illustrates a conventional
5   implantable infusion device for delivering an infusate
at a prescribed rate incorporating a passive pumping
mechanism;

FIGURE 2A schematically illustrates an implantable
infusion device in accordance with one embodiment of
10   the present invention, FIGURE 2B schematically
illustrates an implantable infusion device in
accordance with another embodiment of the present
invention, and FIGURE 2C schematically illustrates an
implantable infusion device in accordance with another
15   embodiment of the present invention;

FIGURE 3 illustrates an exemplary timing chart
corresponding to valve control for regulating a
delivery of infusate from an infusate reservoir of the
implantable infusion device of either FIGURE 2A, 2B, or
20   FIGURE 2C;

FIGURE 4 schematically illustrates an implantable
infusion device in accordance with another embodiment
of the present invention;

FIGURE 5 partially illustrates a schematic
25   representation of an implantable infusion device in
accordance with another embodiment of the present
invention;

FIGURE 6 partially illustrates a schematic
representation of an implantable infusion device in
30   accordance with another embodiment of the present
invention;

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FIGURE 7 partially illustrates a schematic representation of an implantable infusion device in accordance with another embodiment of the present invention;

5   FIGURE 8 partially illustrates a schematic representation of an implantable infusion device in accordance with another embodiment of the present invention;

FIGURE 9 partially illustrates a schematic

10   representation of an implantable infusion device in accordance with another embodiment of the present invention;

FIGURE 10 partially illustrates a schematic representation of an implantable infusion device in

15   accordance with another embodiment of the present invention; and

FIGURE 11 partially illustrates a schematic representation of an implantable infusion device in accordance with another embodiment of the present

20   invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Various embodiments, including preferred embodiments, will now be described in detail below with reference to the drawings.

25   FIGURE 1 illustrates a conventional, constant flow rate infusion device 10. The device 10 is characterized by an infusate reservoir 12 that is required to store a prescribed volume of infusate, e.g., insulin, medicament, pain relieving drugs, etc.

30   The infusate reservoir 12 is of sufficient volume so as to provide a supply of infusate (i.e., a prescribed dose (D)) over a flow period (τ) at a (theoretically)

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constant flow rate. As but one possible example, the
volume of the infusate reservoir 12 can be fixed at any
prescribed volume to enable delivery of a precisely
controlled volume of infusate from one day to more than
5   three months. The infusate reservoir 12 can be
refilled through a septum 14.

Infusate is pressurized and thereby driven from
the infusate reservoir 12 by a drive source 16. The
physical nature of the drive source 16 can be a two-
10   phase fluid, which is confined between the housing of
the device 10 and a movable diaphragm structure 18, a
drive spring that forms the diaphragm structure 18, or
like mechanisms/structures that develop a substantially
constant pressure. A flow restrictor 20 is positioned
15   downstream from the infusate reservoir 12 to establish
an output flow rate. The flow restrictor 20 can be
constructed of any number of potential structures, for
example, a plate having a groove formed therein,
capillary tubing, an etched flow chip, or the like.
20   Although not shown, a filter is preferably
interpositioned between the infusate reservoir 12 and
the restrictor 20 to prevent any bacteria present in
the infusate reservoir 12 from being transferred into
the body, and to a certain extent, to protect the
25   restricted flow path defined by the restrictor 20.
Flow from the flow restrictor 20 is passed to a
catheter 22 having its distal end positioned at a site
for fluid delivery.

Conventional implantable infusion devices can
30   further include a bolus port structure 24. The bolus
port structure 24, whether integral with the device 10
or separate therefrom, provides direct fluid

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communication with the catheter 22. The bolus port
structure 24 is adapted to receive independently a
hypodermic needle (or cannula). Fluid delivered to the
bolus port structure 24 can be used to flush the
5   downstream catheter 22, deliver a prescribed dosage of
medicament (possibly of a volume greater or at a rate
greater than that otherwise capable to be delivered
through the flow restrictor 20), or perform
troubleshooting or diagnostic procedures. Depending on
10   the configuration of the bolus port structure 24, the
structure 24 can also allow extraction of fluid from
the patient via the catheter 22.
      FIGURE 2A illustrates one embodiment of the
present invention. Specifically, an implantable
15   infusion device has a infusate reservoir 12 connected
between a septum 14 and a flow restrictor 20. Infusate
within the infusate reservoir 12 is pressurized and
thereby driven through the flow restrictor 20 by the
drive source 16. The illustrated infusion device
20   includes a first pressure sensing device 24, to measure
a pressure upstream of the flow restrictor 20, and a
second pressure sensing device 26, to measure a
pressure downstream of the flow restrictor 20.
Respective positions of the pressure sensing devices 24
25   and 26 relative to a flow path through the infusion
device are not critical so long as the pressure sensing
device 24 remains upstream of the flow restrictor 20
and the pressure sensing device 26 remains downstream
of the flow restrictor 20. Alternatively, given that
30   the flow rate will be determined by a pressure
differential (ΔP) at the point of the pressure sensing

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devices 24 and 26, it is also possible to measure this
pressure differential (ΔP) with a single pressure
transducer, operatively coupled to the flow path at or
about the same two points as otherwise occupied by the
5   pressure sensing devices 24 and 26 (FIGURE 2A or FIGURE
4) or as otherwise occupied by the pressure sensing
devices 24 and 40 (FIGURE 4), as illustrated in FIGURES
2B and 2C.

It will be readily apparent to those of ordinary
10 skill in the art that a multitude of configurations are
within the scope of the present invention, such
configurations including at least one flow restrictor,
one pressure sensor, and a mechanism to change the
total flow resistance of the system. To this end,
15 FIGURES 2A to 11 illustrate some of the possible
configuration-combinations that includes: (i) one or
more flow restrictors arranged in parallel, series, or
combinations thereof; (ii) one or more valves, whereby
these elements can affect an overall flow resistance;
20 and (iii) one or more pressure sensors that are capable
of determining a pressure difference across any portion
of or all of the flow restrictors or valves. In regard
to (ii) above, depending upon the intended use of the
infusion device, it may be desirable to use fixed or
25 variable flow restrictors, which includes mono-stable,
bi-stable, or multi-stable valves that have the
potential of occluding or partially occluding the
possible flow paths.

A valve 28 is positioned downstream of the flow
30 restrictor 20, and is preferably positioned downstream
of the pressure sensing device 26. Accordingly, the

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pressure sensing device 24 can be positioned within or
proximate to the infusate reservoir 12, and the
pressure sensing device 26 can be positioned subsequent
to the valve 28.

5   A controller 30 (e.g., a microprocessor) is
electrically connected to the pressure sensing device
24, the pressure sensing device 26, and the valve 28.
The controller 30 functions to control fluid flow
through the valve 28 based on respective outputs from
10   pressure sensing devices 24 and 26.

A fluid flow rate across the flow restrictor 20
can be calculated from:

$$Q = (P_R - P_D) \div R$$

where,

15   Q is a flow rate output from the catheter 22;

P_R is a measured reservoir pressure;

P_D is a measured delivery pressure; and

R is a flow resistance value of the flow path as a
whole, which can be approximated by the resistive value
20   of the flow restrictor 20 (when the valve is in an open
state).

An optional temperature sensing device 38 can also
be coupled to the controller 30. If provided, the
controller 30 would function to control fluid flow
25   through the valve 28 also in consideration of (or
solely based on) an output from the temperature sensing
device 38. The controller 30 is adapted to relate
changes in an infusate temperature to proportional
changes in system pressure and/or to changes in the
30   resistive value (R), the latter being caused by a
change in fluid viscosity due to a change in infusate
temperature. This ability of the controller 30 is

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managed by algorithms or look-up tables stored in
memories 32 and/or 34.

A flow cycle of an infusion device is considered
to extend through the delivery of the contents of the
5   infusate reservoir 12, i.e., from a refilling event
until a subsequent refilling event. The quantity (S)
of active pharmacological agents or other agents
(individually or collectively "agent") contained in the
infusate reservoir 12 depends upon the fluid volume (V)
10   of the infusate reservoir 12 and the concentration of
the agent in the infusate stored therein:

$$S = V * C$$

where,

S is the quantity (e.g., mg) of the agent,
15   C is the agent concentration in the infusate
contained in the infusate reservoir 12, and

V is the fluid volume of the infusate reservoir
12.

The duration of the flow cycle is referred to as
20   the flow period (τ). As is probable, the flow period
will typically be between 1 and over three (3) months.
It is related to the flow rate (Q) and the infusate
reservoir volume (V) as follows:

$$\tau = V \div Q$$

25   where,

τ is the flow period (e.g., days), and

Q is the infusate flow rate (e.g., ml/day).

A prescribed (or desired) dose (D) delivered must
be further calculated in accordance with the following:
30   $$D = Q * C$$

where,

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D is the quantity of an agent delivered per unit
of time (e.g., mg/day).

As discussed above, conventional constant flow infusion
devices deliver a single prescribed dose (D) based on
5   the assumption that a constant pressure is maintained
over an entire flow period (τ). As also discussed
above, this assumption can be realistically compromised
by changes in ambient pressure or temperature, patient
position, or infusate volume residing in the reservoir
10 throughout a flow period (τ). Moreover, the total flow
resistance (R) provided by the flow path can change
over the lifetime of the infusion device further
affecting the discharge performance of the device.
Moreover, the properties of the infusate can change
15 over the lifetime of the infusion device, further
affecting the therapy.

In contrast, the devices of the present invention
seek to provide the desired flow accuracy in spite of
the fact that the pressure differential (ΔP) and/or
20 flow resistance (R) may not remain constant over the
entire flow period (τ). These devices do this by
subdividing the flow period (τ) into smaller unit dose
periods ($t_{i,j}$) over which the flow parameters (ΔP) and
(R) are likely to remain constant and delivering the
25 total dose (D) though a series of sequential unit dose
periods ($t_{i,j}$). The following definitions and equations
help to understand the present invention.

A flow period (τ) can be subdivided into any
number (n) of prescribed dose periods (T_i), which may
30 or may not be of equal duration. For conventional

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constant flow pumps, n=1. For the present invention,
"n" may be any integer, preferably two or greater.

$$\tau = \sum_{i=1}^{n} T_i$$

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For various embodiments of the present invention,
the duration of the prescribed dose periods (T_i) may or
may not be physician-alterable (i.e., to create a
programmable pump) and/or patient-alterable (i.e., to
10   create a programmable pump with patient-controllable
elements) either before or during the flow period (τ).

During each of the prescribed dose periods (T_i) a
prescribed dose (D_i) is delivered. If all of these
prescribed doses (D_i) are equal, then the equations
15   describe a constant flow infusion device, possibly with
improved flow accuracy such as, for example,
illustrated in FIGURE 2A. If there are multiple
prescribed doses (D_i) of different magnitudes, then the
equations describe a programmable pump operating with a
20   complex continuous infusion pattern. The therapeutic
value of these complex infusion patterns is readily
apparent to clinicians, and varies depending upon the
agent, patient, and application.

In all applications, a certain quantity of drug
25   (s_i) is to be delivered in the dose period (T_i) at a
prescribed dose (D_i). The following equations
illustrate the relationship among these variables,

$$S = \sum_{i=1}^{n} s_i = \sum_{i=1}^{n} D_i * T_i$$

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In the present invention, each of the prescribed dose periods (T_i) is further divided into any number (m_i) of unit dose periods ($t_{i,j}$). For the present invention, "m" may be any integer, one or greater. In
5   a preferred embodiment, all of the unit dose periods ($t_{i,j}$) within a given prescribed dose period (T_i) are equal. This simplifies the calculations necessary for device operation; however, this is not a necessary condition. In general,

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$$T_i = \sum_{j=1}^{m_i} t_{i,j}$$

and,

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$$\tau = \sum_{i=1}^{n} \sum_{j=1}^{m_i} t_{i,j}$$

when all unit dose periods ($t_{i,j}$) within each of the prescribed dose periods (T_i) are equal,

$$T_i = m_i * t_i$$

20   and,

$$\tau = \sum_{i=1}^{n} m_i * t_i$$

During each unit dose period ($t_{i,j}$), the valve 28
25 will be actuated through one complete cycle, such that it is in one position (i.e., designated open) for a fraction of the unit dose period ($t_{i,j}$) and in a second position (i.e., designated closed) for the balance of the unit dose period ($t_{i,j}$). Those skilled in the art
30 will readily appreciate that it would also be possible to use one or more valves to move between two or more

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position during any given unit dose period $(t_{i,j})$, and
it would also be possible for such valve(s) to move
between different positions during the same or
different unit dose periods $(t_{i,j})$.

In the simplified embodiment described herein, the
controller 30 determines a timing for keeping the valve
28 in an open state based on the most recent estimate
or measurement of the flow parameters $(\Delta P_{i,j})$ and $(R_{i,j})$.
The flow parameters are assumed (approximated) to be
constant for at least the period of time that the valve
28 remains in a given position. The following
equations are useful in determining the amount of agent
delivered (s_i) in a prescribed dose period (T_i), and
the prescribed dosage pharmacologically perceived,

$$t_{i,j} = t_{i,j\ open} + t_{i,j\ close}$$

$$s_i = C * \sum_{j=1}^{m_i} \left(t_{i,j\ open} * Q_{i,j\ open} + t_{i,j\ close} * Q_{i,j\ close} \right)$$

$$D_i = (C \div T_i) * \sum_{j=1}^{m_i} \left(t_{i,j\ open} * Q_{i,j\ open} + t_{i,j\ close} * Q_{i,j\ close} \right)$$

where,

$t_{i,j\ open}$ is the duration of time that the valve
28 is in an open state,

$t_{i,j\ close}$ is the duration of time that the
valve 28 is in a closed state,

$Q_{i,j\ open}$ is the flow rate when the valve 28 is
in the open state during unit dose period $t_{i,j}$, and

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$Q_{i,j}$ close is the flow rate when the valve 28 is in the closed state during unit dose period $t_{i,j}$.

For passive pumping devices, the flow rate can be further described by the following equations,

5
$$Q_{i,j \text{ open}} = \Delta P_{i,j \text{ open}} \div R_{i,j \text{ open}}$$

$$Q_{i,j \text{ close}} = \Delta P_{i,j \text{ close}} \div R_{i,j \text{ close}}$$

For restrictor-based passive pumping devices, $\Delta P_{i,j \text{ open}}$ will often be assumed to be equal to $\Delta P_{i,j \text{ close}}$ for any given i,j. Thus, the position of the valve 28

10
simply changes the resistance magnitude (R) from $R_{i,j \text{ open}}$ to $R_{i,j \text{ close}}$. For passive pumping devices incorporating a regulator, $R_{i,j \text{ open}}$ will often be approximated as equal to $R_{i,j \text{ close}}$ and the position of the valve 28 simply

15
changes the magnitude of ΔP from $\Delta P_{i,j \text{ open}}$ to $\Delta P_{i,j \text{ close}}$.

While in many cases $Q_{i,j \text{ close}}$ will be a zero value, i.e., the valve 28 closes completely and flow stops, such is not a necessary condition. For example, if maintaining the valve in an open state uses battery

20
power, then it may be advantageous to design the infusion device to have a non-zero $Q_{i,j \text{ close}}$ flow rate to thereby reduce the amount of time that the valve 28 needs be held open, and thereby conserve battery power. Alternatively, it may be possible to use a longer unit

25
dose period ($t_{i,j}$) when using a non-zero $Q_{i,j \text{ close}}$ flow rate, and thereby reduce battery consumption by reducing the total number of unit dose periods. In cases when $Q_{i,j \text{ close}}$ is zero the equation simplifies to,

30
$$s_i = C * \sum_{j=1}^{n} t_{i,j \text{ open}} * Q_{i,j \text{ open}}$$

23

In a preferred embodiment, the unit dose period $(t_{i,j})$ is pre-determined, and $t_{i,j\ open}$ is calculated to effect the desired agent delivery. Those skilled in the art will readily recognize that it is possible to

5 obtain the same effect by pre-determining $t_{i,j\ open}$ and calculating $t_{i,j\ close}$, and thereby calculating $t_{i,j}$ so that effectively $t_{i,j\ open}$ is held constant while $t_{i,j}$ is varied.

The duration of the unit dose periods $(t_{i,j})$ is so

10 chosen so that they are: (i) short enough that the flow parameters (ΔP) and (R) are unlikely to change significantly so that the flow rates $Q_{i,j\ open}$ and $Q_{i,j\ close}$ can be approximated as being constant over the unit dose period $(t_{i,j})$; (ii) short enough that the

15 open/close flow rate changes are pharmacologically imperceptible or insignificant; and (iii) long enough to achieve acceptable levels of battery consumption (by minimizing the number of battery-consuming opening and closing cycles for the valve 28).

20 The above algorithms are maintained in non-volatile memory 32, and RAM 34 is used as a work space for at least the purposes of the above calculations. The controller 30 is further coupled to an internalized power source 36.

25 Reference is hereby made to FIGURE 3, which illustrates but one example of the control signals delivered from the controller 30 to the valve 28. The illustrated signals extend over a period of time in which the potential output flow rate decreases. For

30 the exemplary illustrated unit dose periods $(t_{i,j})$, the duration of $t_{1,x\ open}$ is increased relative to the

24

duration of, for example, $t_{1,1\ open}$ for the "initial" dose periods ($t_{i,j}$). Notwithstanding, the duration of the unit dose period ($t_{1,m}$, $= t_1$ for all of m) is held constant. Of course, the noted change in $t_{i,j\ open}$

5   compensates for the change in infusate flow rate without express regard for the reason for such change in flow rate.

    In some devices the pressure generated by the drive source 16 will vary according to the volume of

10   infusate remaining in the infusate reservoir 12. For example, in many devices the reservoir pressure drops as the reservoir volume is nearly depleted and rises as the reservoir volume nears (or exceeds) its rated capacity. In conventional infusion devices this is a

15   liability because it affects and therefore reduces the flow rate accuracy and the usable volume of the infusate reservoir 12. However, in the present invention this information can be an asset that is used: (i) in the case of filled reservoirs, to alert a

20   user so as to prevent a dangerous or undesirable overfilling of the pump; and/or (ii) in the case of nearly depleted reservoirs, to measure the volume of fluid remaining in the infusate reservoir 12 by measuring the reservoir pressure, and if appropriate,

25   alert a user that the device should be refilled. As described earlier, the controller can use this information to adjust the open/close cycles, and thereby extend the usable volume of the infusion device without changing the physical size of the device.

30   In some clinical applications, the duration of the flow period (τ) can be limited by the compatibility or

25

stability of an active agent in the infusate.
"Compatibility" and "stability" are terms that are
intended to capture all of the changes that can occur
in the chemical, physical, pharmacological, or

5   therapeutic properties of an infusate as it resides
inside the infusate reservoir 12 of the drug delivery
device. While not exhaustive, these changes include:
(i) a decrease in the potency of the active ingredient;
(ii) an increase in the potency of the active

10   ingredient; and (iii) a change in infusate viscosity.
For example, the potency of morphine sulfate in
conventional implantable infusion pumps is known to
decrease by about 20% over a 90 day period, thus the
lack of morphine stability restricts the maximum flow

15   period for this agent to less than about 90 days
(without regard to a potential volumetric capacity of
the delivering infusion device). This fact, as well as
the fact that some conventional constant flow
implantable infusion pumps flow faster when full then

20   they do when nearly empty, means that the actual drug
dose received by the patient can vary dramatically over
a flow period (τ).

However, in the present invention look up tables
or algorithms can be used to compensate for known

25   changes in the properties of the infusate to adjust the
flow controller over the course of the flow period (τ).
This has at least two beneficial effects: (i) a more
uniform amount of active agent is administered
throughout the flow period (τ), thereby improving

30   therapy and/or reducing side effects; and (ii) the

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maximum duration of the flow period (τ) can be extended
so that more of the infusate reservoir can be used.

For any internally powered, implantable device,
the life span of its power source dictates its
5   functional life. Of course, removal and replacement of
such device can be traumatic, as the patient is
required to undergo a surgical procedure to effect such
removal and replacement. As the benefits of any such
implantable device are carefully weighed against the
10   costs of use/replacement (e.g., hardware expense,
physician time, hospitalization, etc.) as well as
patient morbidity/mortality, it is imperative that
efforts be made to provide an implantable device
capable of sustaining sufficient operational life but
15   remain cost and size effective. Even when the device
incorporates a rechargeable power source (e.g.,
battery, capacity, etc.) minimizing power consumption
is desirable.

System power consumption is largely dictated by
20   the power consumed to actuate the valve 28 through each
open-close cycle for each unit dose $(d_{i,j})$ and
generally, to a lesser extent, by that required to make
the measurements and calculations required to control
the valve timing. It is an objective of the present
25   invention to safely minimize and control a total
current drain associated with the operation of the
valve 28. This control increases the predictability of
a life-span of a power source (36, FIGURES 2A, 2B, and
2C). A generalized equation for current drain
30   resulting from valve actuation for one unit dose cycle
$(t_{i,j})$ is:

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$$I_{total} = I_{open} + I_{held\ open} \cdot t_{i,j\ open} + I_{close} +$$
$$I_{held\ close} \cdot t_{i,j\ close}$$

where,

for a bi-stable valve, $I_{held\ open}$ and $I_{held\ close}$

5   are zero values, thus $I_{total} = I_{open} + I_{close}$; and by

comparison,

for a mono-stable valve, I_{close} and $I_{held\ close}$

are likely zero values, thus $I_{total} = I_{open} + I_{held\ open} \cdot t_{i,j}$

$_{open}$.

10   From the above examples, it can be readily seen

that system current drain can be easily approximated

from the operative nature of a selected valve, wherein

the basis for valve selection depends upon an intended

application.

15   Shortening the duration of the unit dose period

($t_{i,j}$) improves flow accuracy, but at the expense of

additional battery consumption to effect incremental

valve actuation, computations, and pressure and/or

temperature measurements. It will also be readily

20   apparent that for reasons of battery conservation,

there may be times and conditions within a given flow

period (τ) when the prescribed dose period (T_i) and/or

unit dose period $(t_{i,j})$ should be lengthened or

shortened, and that based on the design of the device

25   it may be possible to predetermine these times (such as

when the infusate reservoir is nearly empty), or to

determine them in real time based on the input from a

sensor. For example, when the reservoir is nearly

depleted, ΔP may change quickly meaning that the unit

30   dose period ($t_{i,j}$) should be shortened to improve flow

accuracy. Doing so, also effectively increases the

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amount of fluid from the infusate reservoir 12 that can be delivered within flow accuracy specifications (i.e., the usable volume), which is a very desirable feature.

Based on a flow rate determined by the controller

5   30, an accurate, dynamic calculation of remaining power source life can be made. Likewise, an estimated life for the power source 36 can be approximated from anticipated changes of the infusion device, or the present invention can be configured to pass calculated,

10   real-time information outside the patient to an external controller 50. For this concept, reference is made to FIGURE 4, which illustrates a second embodiment of the present invention.

Controller 50 communicates with the controller 30

15   through a patient's skin. Such communication is made, for example, using common radio-frequency technology that is well known in the art. The manner and form of communication is not critical. Any means (e.g., IR, direct connection, etc.) that is capable of

20   establishing a data transfer link, provided that the controller 50 and the implantable infusion device are provided with the proper link components, is consistent with this aspect of the disclosed invention.

The controller 50 can provide information (e.g.,

25   software updates, modification of calculation variables, for example, the unit dose period $(t_{i,j})$, $t_{i,j}$ open, etc.) to the controller 30 for maintaining accurate functionality of the infusion device. Moreover, the controller 50 can provide instructions to

30   the controller 30 to change any of these variables in response to changes in other parameters, e.g., complex continuous infusion. The controller 50 could also

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transmit power to the power source 36, if the power
source 36 was of a rechargeable nature. Further yet,
the controller 50 could transmit power directly to the
controller 30 via a carrier signal, e.g., using a
5   radio-frequency carrier signal.

It is contemplated that through the communication
link between the controller 30 and the controller 50,
data can be uploaded from the controller 30 to the
controller 50. To this end, the controller 50
10   preferably includes a display 50a, which can
communicate information, e.g., life expectancy of the
power source 28, to a user for real-time consideration.
Additionally, diagnostic information regarding the
operability of the implantable infusion device can be
15   supplied to the user with only slight modification to
the system illustrated in FIGURE 2A.

In further reference to FIGURE 4, an infusion
device in accordance with the present invention could
be provided with a third pressure sensing device 40,
20   which is positioned downstream of the valve 28.
Further yet, additional variations of the specific
arrangement of the components of this system are
illustrated in FIGURES 5-11.

From the initial pressure sensing devices 24 and
25   26 (and the optional third pressure sensing device 40),
the following information can be gathered and supplied
back to a monitoring user via a data link between the
controller 30 and the controller 50:

Valve open, if $P_R > P_{D1} \cong P_{D2}$;

30   Valve closed, if $P_R \cong P_{D1} > P_{D2}$;

30

Catheter obstruction (e.g., kink, thrombosis), if $P_R \cong P_{D1} \cong P_{D2}$

Further yet, transient responses from the second pressure sensing device 26 and the third pressure
5   sensing device 40 during or proximate to an opening or closing of the valve 28 can be monitored to provide information regarding a system status. For example, in reference to the exemplary embodiment illustrated in FIGURE 4, if prior to opening the valve 28, $P_R \cong P_{D1} \geq$
10   P_{D2}, then as the valve 28 is opened, a measured pressure transient enables a calculated appreciation of how freely infusate is able to flow through the catheter 22 and the flow restrictor 20. The rate of change of pressures P_{D1} and P_{D2} will communicate whether
15   or not certain parts of the flow path are obstructed (e.g., completely or in part), and if obstructed, the location of such obstruction relative to the flow path. Moreover, as the valve 28 is closed, a measured pressure transient (between P_{D1} and P_{D2}) will allow an
20   inference as to how freely infusate is able flow from the infusate reservoir 12 through at least the restrictor 20. A rate of change of pressure will communicate whether the system filter (positioned between the infusate reservoir 12 and the restrictor
25   20) or the restrictor 20 is partially or completely obstructed as might occur over the lifetime of the device. Of course, this information could be displayed on the display 50a. In a like manner, as the valve 28 is closed, a pressure transient measured for P_{D2} will
30   allow an inference as to how freely infusate is able to flow through the delivery catheter 22.

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Provided that the critical portion of the flow
path (i.e., that portion through which regardless of
any/all valve states all infusate must flow) within the
infusion device 10 is not completely occluded, the data
gained from the aforementioned detected conditions can
enable a modification of controller variables (e.g.,
the unit dose period $(t_{i,j})$, $t_{i,j\,open}$, etc.) so as to
enable a targeted dosage/delivery rate to be
maintained. The information gained can also provide
the managing clinician with valuable information to
help determine whether or not surgical intervention or
a change in dosage is required.

As should also be noted, while the controller 50
has been described as a device capable of establishing
a data transfer link, it should be further noted that
modification of at least calculation variables (e.g.,
the unit dose period $(t_{i,j})$, $t_{i,j\,open}$, etc.) can be
accomplished through other non-invasive methods (e.g.,
magnetic switch control) or invasive methods (e.g.,
trocar).

While the invention has been described herein
relative to a number of particularized embodiments, it
is understood that modifications of, and alternatives
to, these embodiments, in particular, variants in the
number, type, and configuration of the flow
restrictor(s), valve(s), and sensor(s), such
modifications and alternatives realizing the advantages
and benefits of this invention, will be apparent those
of ordinary skill in the art having reference to this
specification and its drawings. It is contemplated
that such modifications and alternatives are within the
scope of this invention as subsequently claimed herein,

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and it is intended that the scope of this invention
claimed herein be limited only by the broadest
interpretation of the appended claims to which the
inventors are legally entitled.

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WHAT IS CLAIMED IS:

1.   An infusion device for implantation in a
living body, the device comprising:

        at least one variable-volume chamber to receive

5   and transiently store a fluid infusate;

        at least one inlet conduit, wherein each variable-
volume chamber is in fluid communication with an inlet
conduit;

        an energy source to effect an expulsion of stored

10   infusate from the at least one variable-volume chamber;

        at least one outlet conduit, in fluid
communication with the chamber(s), to facilitate the
passage of infusate from the chamber(s) to a delivery
site; .

15   a flow resistor network including at least one
flow restrictor positioned relative to the outlet
conduit;

        at least one pressure sensing device to measure a
pressure differential across at least a portion of the

20   flow restrictor network;

        at least one valve, positioned relative to the
outlet conduit, to selectively control an infusate
output from the device; and

            a controller, coupled to the at least one

25   pressure sensing device and to the at least one valve,
to control an operation of the at least one valve based
on measured values obtained by the at least one
pressure sensing device.

30   2.   A device in accordance with Claim 1, wherein
a first pressure sensing device, which is one of the at
least one pressure sensing device, is adapted to

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measure an infusate pressure across the at least one
valve.

    3.   A device in accordance with Claim 1, wherein
5   a first pressure sensing device is adapted to measure
an infusate pressure prior to the at least one flow
restrictor, and a second pressure sensing device is
adapted to measure an infusate pressure subsequent to
the at least one flow restrictor, and wherein the first
10 pressure sensing device and the second pressure sensing
device are two of the at least one pressure sensing
device.

    4.   A device in accordance with Claim 1, further
15 comprising a temperature sensor to measure an infusate
temperature, and the controller is further coupled to
the temperature sensor.

    5.   A device in accordance with Claim 4, wherein
20 the controller is adapted to control the at least one
valve based also on measured values obtained by the
temperature sensor.

    6.   An infusion device for implantation in a
25 living body having a collapsible infusate chamber, an
energy source to collapse the chamber, and an outlet
flow path extending between the chamber and a device
outlet having a flow resistance, the device comprising:
     a pressure sensing mechanism to measure an
30 infusate pressure differential across at least a
portion of the flow resistance;

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a valve, which defines at least in part the flow
resistance, to selectively obstruct the outlet flow
path; and

a controller, coupled to the pressure sensing
5   mechanism and the valve, to control an operation of the
valve based on measured values obtained by the pressure
sensing mechanism,

wherein a prescribed dose to be delivered by the
device consists of a plurality of unit dose cycles,
10   each unit dose cycle being defined by an open-close
cycle of the valve, and

wherein the controller is adapted to regulate an
operational timing of the open-close cycle of the valve
to deliver a constant unit dose amount for each dose
15   cycle.

7.   A device in accordance with Claim 6, further
comprising a flow resistor, which defines at least in
part the flow resistance, positioned relative to the
20   outlet conduit.

8.   A device in accordance with Claim 7, wherein
the pressure sensing mechanism includes a first
pressure sensing device to measure an infusate pressure
25   upstream of the flow restrictor and a second pressure
sensing device to measure an infusate pressure
downstream of the flow restrictor.

9.   A device in accordance with Claim 6, wherein
30   the pressure sensing mechanism is further adapted to
measure an infusate pressure across the valve.

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10. A device in accordance with Claim 6, further comprising a temperature sensor to measure an infusate temperature, and the controller is further coupled to the temperature sensor.

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11. A device in accordance with Claim 10, wherein the controller is adapted to control the valve based also on measured values obtained by the temperature sensor.

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12. A device in accordance with Claim 6, wherein the controller varies a duty cycle of the open-close cycle of the valve within a prescribed cycle period.

15   13. A device in accordance with Claim 6, wherein the controller varies a period of the open-close cycle.

14. An infusion device for implantation in a living body having a collapsible infusate chamber to
20 transiently store an active agent-containing infusate, an energy source to collapse the chamber, and an outlet flow path extending between the chamber and a device outlet having a flow resistance, the device comprising:
        a pressure sensing mechanism to measure an
25 infusate pressure differential across at least a portion of the flow resistance;
        a valve, which defines at least in part the flow resistance, to selectively obstruct the outlet flow path; and
30   a controller, coupled to the pressure sensing mechanism and the valve, to control an operation of the

valve based on measured values obtained by the pressure
sensing mechanism,

wherein a prescribed dose, to be delivered over a
prescribed dose period, consists of a plurality of unit

5   dose cycles, each unit dose cycle being defined by an
open-close cycle of the valve, and

wherein the controller is adapted to regulate an
operational timing of the open-close cycle of the valve
to compensate for changes in the active agent-

10   containing infusate, thereby maintaining a prescribed
dose of active agent over the prescribed dose period.

15.   A device in accordance with Claim 14, wherein
the operational timing that is subject to regulation by

15   the controller is a duty cycle of the open-close cycle
of the valve.

16.   An infusion device for implantation in a
living body having a collapsible infusate chamber to

20   transiently store an active agent-containing infusate,
an energy source to collapse the chamber, and an outlet
flow path extending between the chamber and a device
outlet having a flow resistance, the device comprising:

a temperature sensing device to measure an

25   infusate temperature;

a valve, which defines at least in part the flow
resistance, to selectively obstruct the outlet flow
path; and

a controller, coupled to the temperature sensing
30   device and the valve, to control an operation of the
valve based on measured values obtained by the
temperature sensing device,

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wherein a prescribed dose, to be delivered over a
prescribed dose period, consists of a plurality of unit
dose cycles, each unit dose cycle being defined by an
open-close cycle of the valve, and

5   wherein the controller is adapted to regulate an
operational timing of the open-close cycle of the valve
based on a change in infusate temperature measured by
the temperature sensing device.

10   17.   A device in accordance with Claim 16, wherein
the operational timing that is subject to regulation by
the controller is a duty cycle of the open-close cycle
of the valve.

15   18.   An infusion device for implantation in a
living body having a collapsible infusate chamber to
transiently store an infusate, an energy source to
collapse the chamber, and an outlet flow path extending
between the chamber and a device outlet having a flow
20   resistance, the device comprising:
         a pressure sensing mechanism to measure an
infusate pressure differential across at least a
portion of the flow resistance;
         a valve, which defines at least in part the flow
25   resistance, to selectively obstruct the outlet flow
path; and
         a controller, coupled to the pressure sensing
mechanism and the valve, to control an operation of the
valve based on measured values obtained by the pressure
30   sensing mechanism,
         wherein a prescribed dose, to be delivered over a
prescribed dose period, consists of a plurality of unit

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dose cycles, each unit dose cycle being defined by an
open-close cycle of the valve, and

    wherein the controller is adapted to regulate an
operational timing of the open-close cycle of the valve

5   based on a change in flow resistance.

    19. A device in accordance with Claim 18, wherein
the operational timing that is subject to regulation by
the controller is a duty cycle of the open-close cycle

10 of the valve.

    20. An infusion device for implantation in a
living body having a collapsible infusate chamber to
transiently store an infusate, an energy source to

15 collapse the chamber, and an outlet flow path extending
between the chamber and a device outlet having a flow
resistance, the device comprising:

    a pressure sensing mechanism to measure an
infusate pressure differential across at least a

20 portion of the flow resistance;

    a valve, which defines at least in part the flow
resistance, to selectively obstruct the outlet flow
path; and

    a controller, coupled to the pressure sensing

25 mechanism and the valve, to control an operation of the
valve based on measured values obtained by the pressure
sensing mechanism,

    wherein a prescribed dose, to be delivered over a
prescribed dose period, consists of a plurality of unit

30 dose cycles, each unit dose cycle being defined by an
open-close cycle of the valve, and

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wherein the controller is adapted to selectively regulate an operational timing of the open-close cycle of the valve in accordance with a volume then-determined to be present within the infusate chamber.

5

21. A device in accordance with Claim 20, wherein the operational timing that is subject to regulation by the controller is a duty cycle of the open-close cycle of the valve.

10

22. An infusion device for implantation in a living body having a collapsible infusate chamber, an energy source to collapse the chamber, and an outlet flow path, having a flow resistance, that extends

15   between the chamber and a device outlet, the device comprising:

a flow restrictor, positioned relative to the outlet flow path, which defines in part the flow resistance;

20   a valve, which defines in part the flow resistance, to selectively obstruct the outlet flow path;

a pressure sensing device to measure an infusate pressure across at least a portion of the flow

25   resistance; and

a controller, coupled to the pressure sensing device and the valve, to control an operation of the valve to selectively obstruct the outlet flow path,

wherein the controller is adapted to assess

30   whether the flow resistance has undesirably changed based on measured values obtained from the pressure sensing device.

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23. A device in accordance with Claim 22, wherein the pressure sensing mechanism includes a first pressure sensing device to measure an infusate pressure

5   upstream of the valve and a second pressure sensing device to measure an infusate pressure downstream of the valve.

24. A device in accordance with Claim 22, wherein

10 the pressure sensing mechanism is further adapted to measure an infusate pressure across the flow restrictor, and the controller is adapted to control the valve based also on measured infusate pressure values across the flow restrictor.

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25. A device in accordance with Claim 22, wherein the controller is adapted to identify a change in the flow resistance upstream of the valve based on measured values obtained from the pressure sensing mechanism.

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26. A device in accordance with Claim 22, wherein the controller is adapted to identify a change in the flow resistance downstream of the valve based on measured values obtained from the pressure sensing

25 mechanism.

27. A method of controlling infusate output from an implantable infusion device for a prescribed dose period, the device having a collapsible infusate

30 chamber, an energy source to collapse the chamber, and an outlet flow path extending between the chamber and a device outlet, wherein the outlet flow path includes a

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restrictor and a valve to selectively and at least partially occlude the outlet flow path, comprising the steps of:

5   dividing the prescribed dose period into a plurality of unit dose periods, wherein each unit dose period is defined by an open-close cycle of the valve; and

modifying a duty cycle of the open-close cycle of the valve so as to maintain a unit dose for each unit
10   dose period.

28.   A method in accordance with Claim 27, wherein the open-close cycle is defined by a fixed period.

15   29.   A method of controlling infusate output from an implantable infusion device for at least one prescribed dose period, the device having a collapsible infusate chamber, an energy source to collapse the chamber, and an outlet flow path extending between the
20   chamber and a device outlet, wherein the outlet flow path includes a restrictor and a valve to selectively and at least partially occlude the outlet flow path, comprising the steps of:

dividing the prescribed dose period into a
25   plurality of unit dose periods, wherein each unit dose period is defined by an open-close cycle of the valve;

measuring an infusate pressure differential across the restrictor; and

modifying an operational timing of the open-close
30   cycle of the valve, in accordance with a measured infusate pressure differential, so as to maintain a unit dose for each unit dose period.

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30. A method in accordance with Claim 29, wherein
a plurality of prescribed dose periods define a flow
period, and further comprising the step of dividing the
5   flow period into the plurality of prescribed dose
periods.

31. A method in accordance with Claim 29, wherein
the operational timing that is subject to regulation by
10   the controller is a duty cycle of the open-close cycle
of the valve.

32. A method in accordance with Claim 29, further
comprising the step of measuring an infusate
15   temperature, wherein the step of modifying is effected
also in accordance with a measured temperature.

33. A method in accordance with Claim 29, further
comprising the steps of:
20   actuating the valve so as to effect a change in an
occluded state of the outlet flow path; and
         measuring a transient pressure profile across the
valve.

25   34. A method in accordance with Claim 33, wherein
the infusion device is adapted to communicate with a
controller external to the patient, and further
comprising the step of transmitting a signal to the
controller, wherein the signal corresponds to the
30   measured pressure profile.

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35. A method in accordance with Claim 33, further
comprising the step of assessing a rate of change of a
measured pressure profile at or about said actuating
step.

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36. A method in accordance with Claim 29, wherein
the infusion device is adapted to communicate with a
controller external to the patient, and further
comprising the step of transmitting a signal to the
10   controller, wherein the signal is representative of the
measured infusate pressure differential.

37. A method of controlling infusate output from
an implantable infusion device for at least one
15   prescribed dose period, the device having a collapsible
infusate chamber to transiently store an active agent-
containing infusate, an energy source to collapse the
chamber, and an outlet flow path extending between the
chamber and a device outlet, wherein the outlet flow
20   path includes a restrictor and a valve to selectively
and at least partially occlude the outlet flow path,
comprising the steps of:
dividing the prescribed dose period into a
plurality of unit dose periods, wherein each unit dose
25   period is defined by an open-close cycle of the valve;
and
modifying an operational timing of the open-close
cycle of the valve to compensate for changes in the
active agent-containing infusate, thereby maintaining a
30   prescribed dose of active agent over the prescribed
dose period.

38. A method in accordance with Claim 37, wherein a plurality of prescribed dose periods define a flow period, and further comprising the step of dividing the flow period into the plurality of prescribed dose
5   periods, and

wherein the step of modifying effects a control over the valve to compensate for changes in the active agent-containing infusate, thereby maintaining a prescribed dose of active agent over each prescribed
10 dose period in the flow period.

39. A method of controlling infusate output from an implantable infusion device for a prescribed dose period, the device having a collapsible infusate
15 chamber, an energy source to collapse the chamber, and an outlet flow path extending between the chamber and a device outlet, wherein the outlet flow path includes a restrictor and a valve to selectively and at least partially occlude the outlet flow path, comprising the
20 steps of:

actuating the valve so as to effect a change in an occluded state of the outlet flow path;

measuring a transient pressure profile across the valve; and

25   assessing a rate of change of the pressure profile during the actuating step.

40. A method in accordance the Claim 39, wherein the step of assessing can reveal an undesired flow
30 restriction upstream of the valve based on a rate of change of a measured pressure profile.

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41.   A method in accordance the Claim 39, wherein the step of assessing can reveal an undesired flow restriction downstream of the valve based on a rate of change of a measured pressure profile.

5

42.   A method in accordance the Claim 39, wherein the step of assessing can reveal a valve malfunction.

43.   A method in accordance the Claim 39, wherein
10 the step of assessing can reveal changes in infusate delivery caused by changes in certain properties of the infusate based on a rate of change of a measured pressure profile, the certain properties being of the group of: physical, chemical, therapeutic, and
15 pharmacological.

44.   A method in accordance the Claim 39, wherein the step of assessing can reveal a catheter malfunction.

20

45.   An infusion device for implantation in a living body, the device comprising:
    a variable-volume chamber to receive and transiently store a fluid infusate;
25   an inlet conduit, which is in fluid communication with the variable-volume chamber;
    an energy source to effect an expulsion of stored infusate from the chamber;
    an outlet conduit, in fluid communication with the
30 chamber, to facilitate the passage of infusate from the chamber to a delivery site;

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a flow restrictor, positioned relative to the outlet conduit, to define a maximum infusate flow rate output from the device;

a first pressure sensing device to measure an
5   infusate pressure upstream of the flow restrictor;

a second pressure sensing device to measure an infusate pressure downstream of the flow restrictor;

a valve to selectively control an infusate output from the device; and
10   a controller, coupled to the first pressure sensing device, the second pressure sensing device, and the valve, to control an operation of the valve based on measured values obtained by the first and second pressure sensing devices.
15
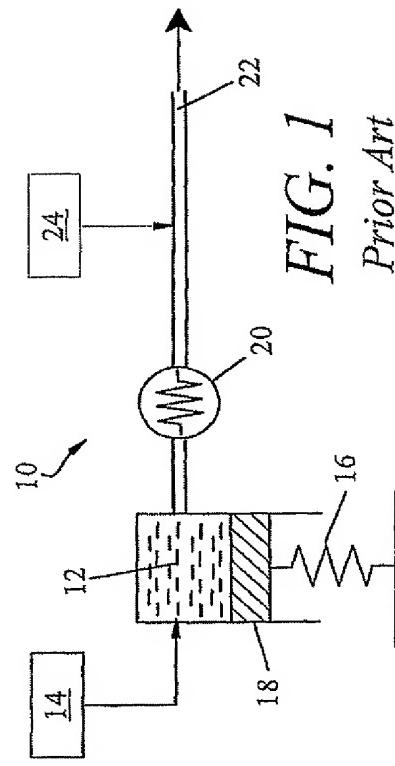
FIG. 1
Prior Art

FIG. 3

FIG. 2A

FIG. 2B

FIG. 2C

FIG. 4

FIG. 5

FIG. 6

FIG. 7

FIG. 8
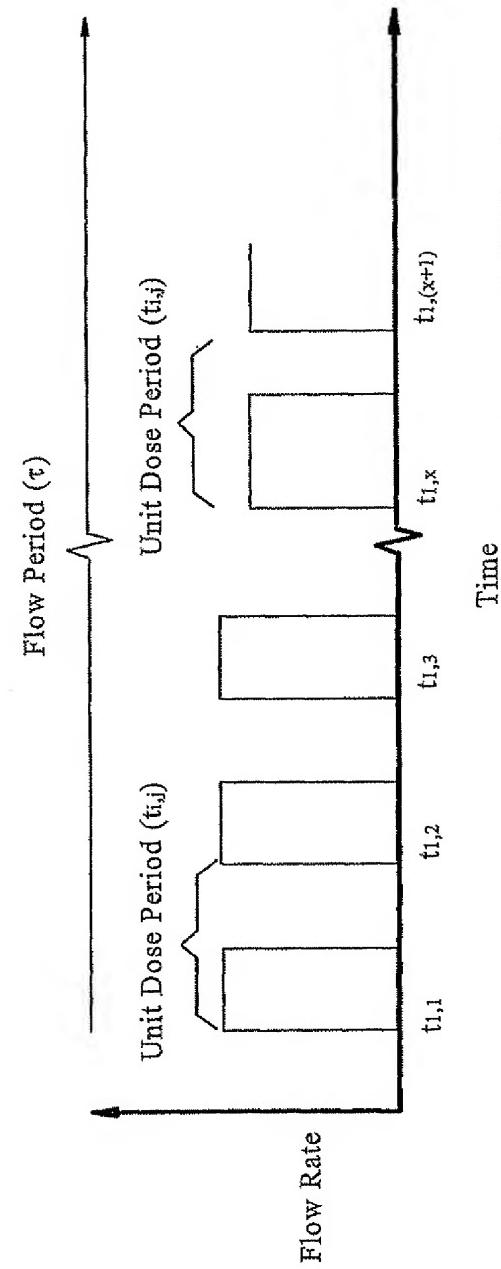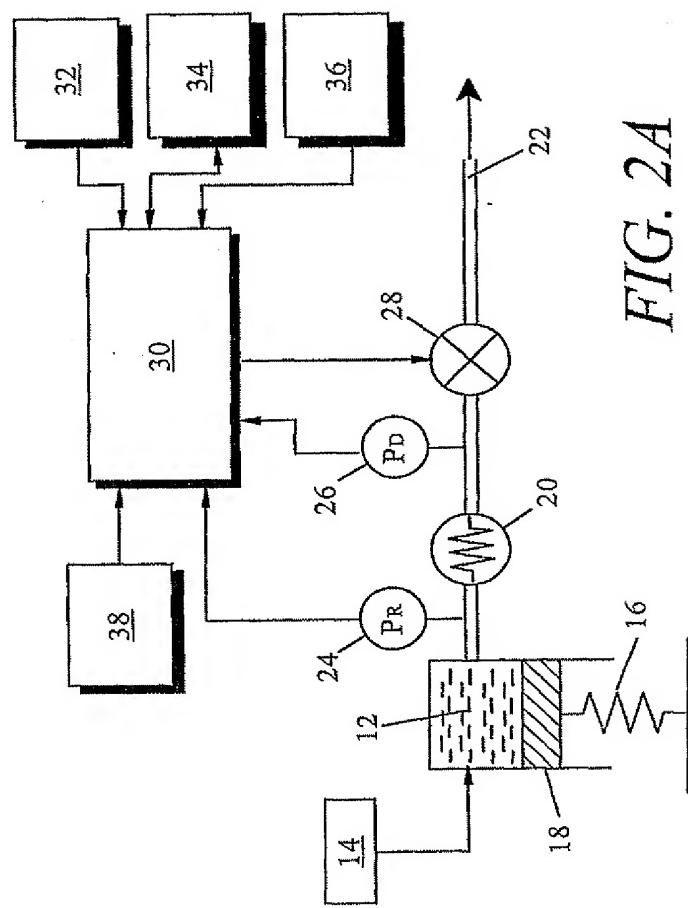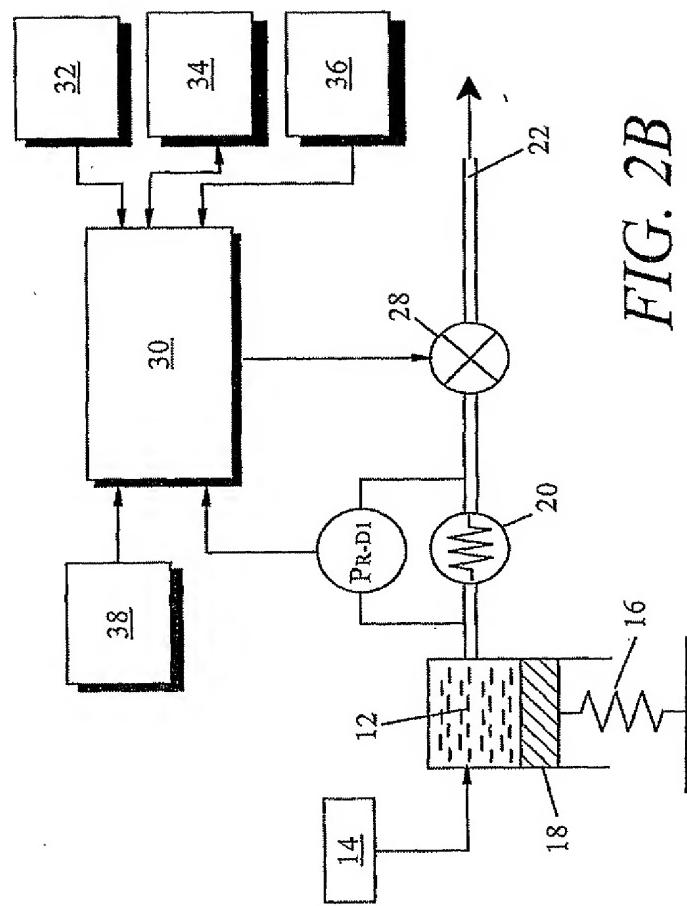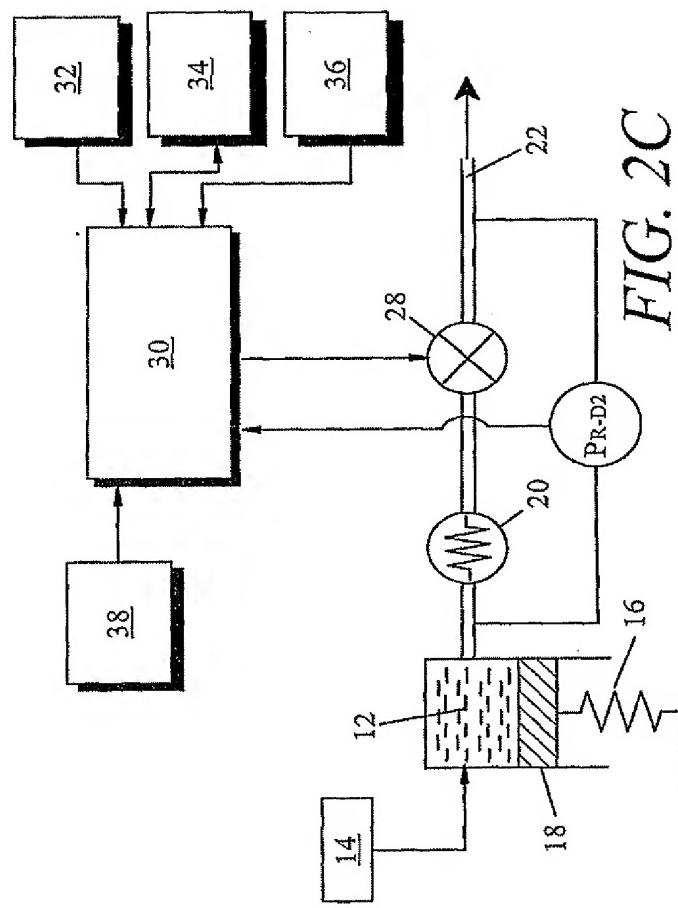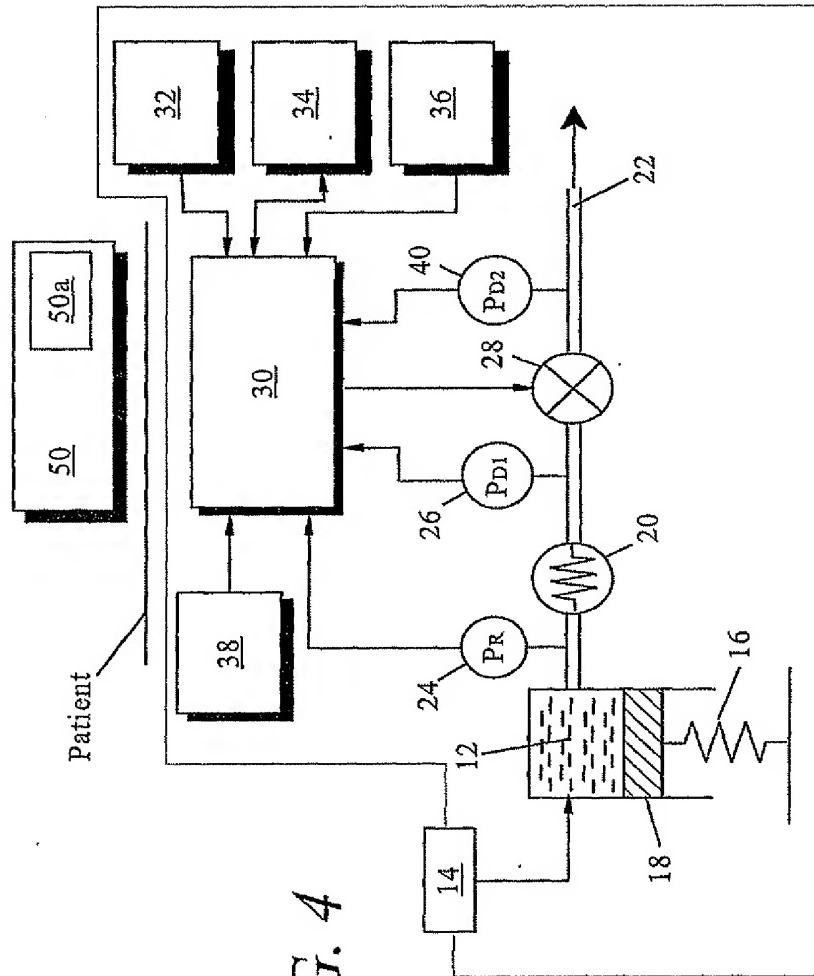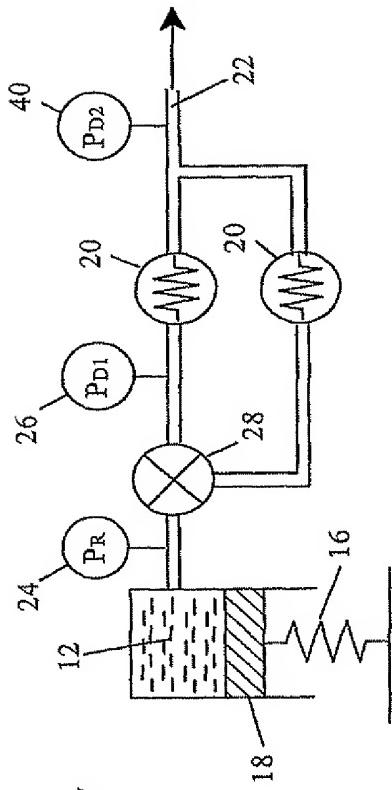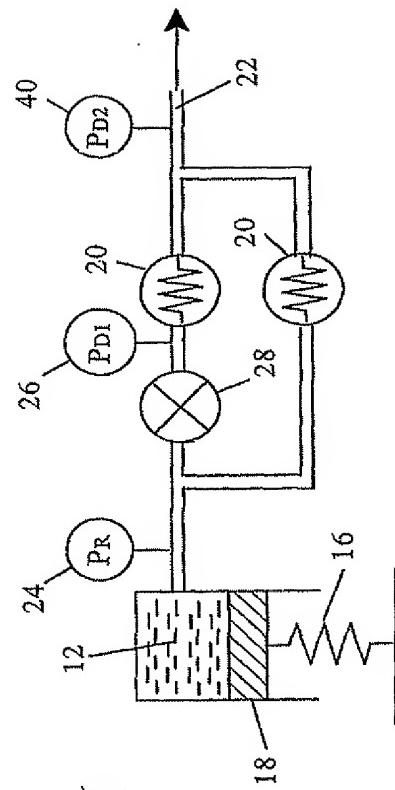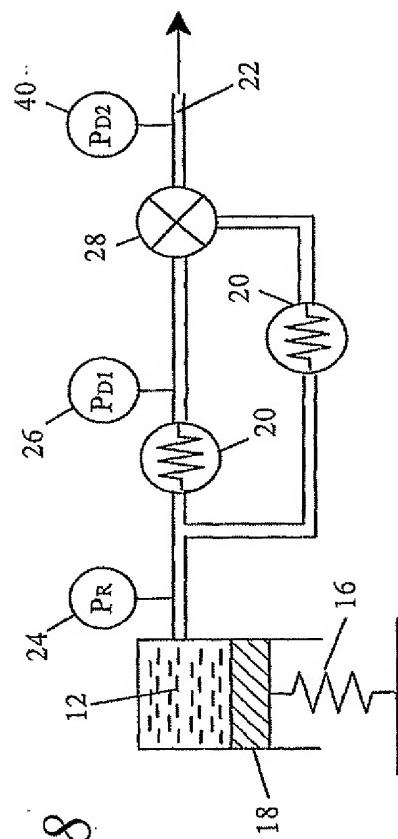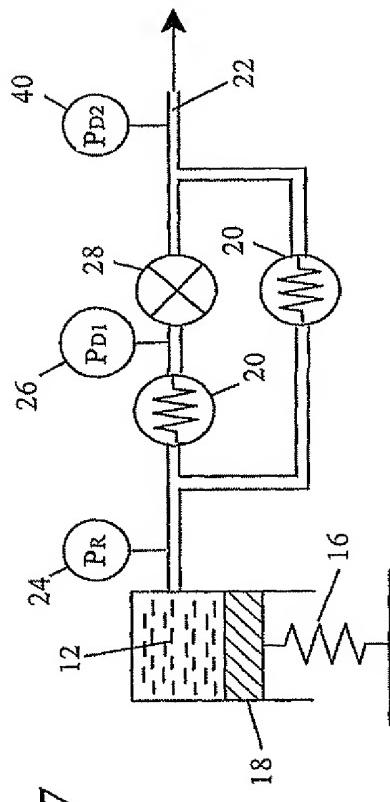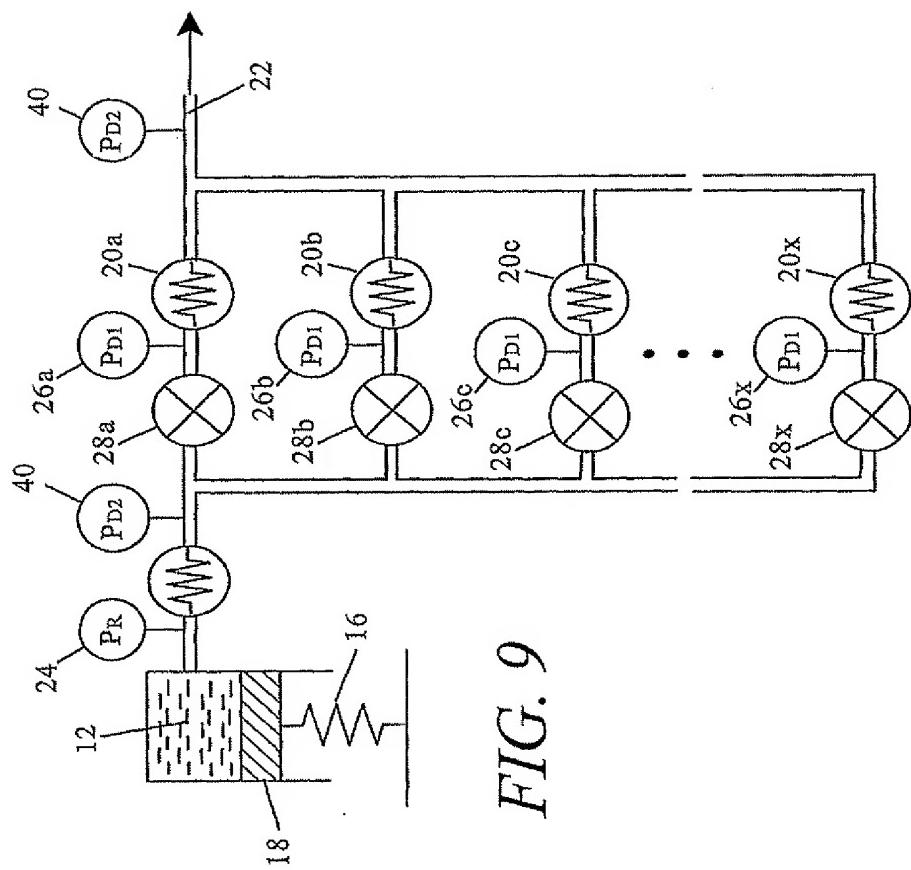
FIG. 9
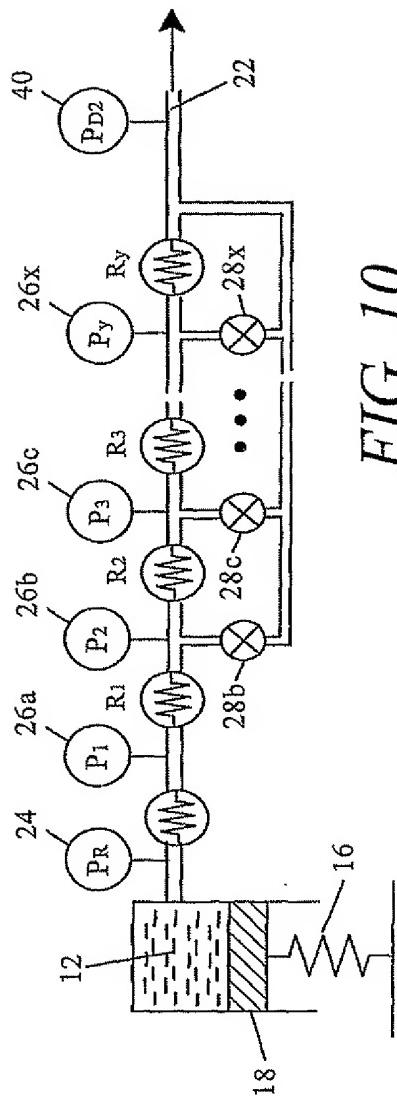
FIG. 10

FIG. 11

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7   A61M5/142   A61M5/145   A61M5/172

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7   A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	DE 100 20 499 A (MEDTRONIC INC) 23 November 2000 (2000-11-23) the whole document	1-45
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A	EP 0 039 124 A (INFUSAID CORP) 4 November 1981 (1981-11-04) the whole document	1-45

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| [X] Further documents are listed in the continuation of box C. | [X] Patent family members are listed in annex. |

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Date of the actual completion of the International search	Date of mailing of the international search report
1 July 2002	11/07/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Nielsen, M

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
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